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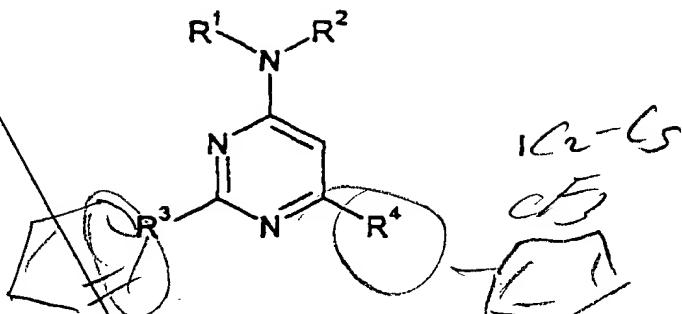
EP009905636

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Patent claims

1. A compound of the formula I,

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in which

R^1 is (C_1 - C_8)-alkyl which can be substituted by one or more identical or different substituents from the group consisting of hydroxyl, (C_1 - C_4)-alkoxy,

10 $R^5 R^6 N$ and aryl, (C_3 - C_9)-cycloalkyl which can be substituted by one or more identical or different substituents from the group consisting of (C_1 - C_4)-alkyl, hydroxyl and amino, or the radical of a 5-membered to 7-membered saturated heterocyclic ring which contains one or two identical or different hetero ring members from the group consisting of O, NR^7 and $S(O)_m$ and which can be substituted by one or more identical or different substituents from the group consisting of (C_1 - C_4)-alkyl and aryl-(C_1 - C_4)-alkyl-;

and

R^2 is hydrogen, (C_1 - C_8)-alkyl which can be substituted by one or more

20 identical or different substituents from the group consisting of hydroxyl, (C_1 - C_4)-alkoxy, (C_1 - C_4)-alkyl- $S(O)_m$, $R^5 R^6 N$ and aryl, (C_3 - C_9)-cycloalkyl which can be substituted by one or more identical or different substituents from the group consisting of (C_1 - C_4)-alkyl, hydroxyl and amino, or the radical of a 5-membered to 7-membered saturated heterocyclic ring which 25 contains one or two identical or different hetero ring members from the group consisting of O, NR^7 and $S(O)_m$ and which can be substituted by one or more identical or different substituents from the group consisting of (C_1 - C_4)-alkyl and aryl-(C_1 - C_4)-alkyl-;

or

30 $R^1 R^2 N$ is a radical, bonded via a ring nitrogen atom, of a 5-membered to 7-membered saturated heterocyclic ring which, in addition to the nitrogen

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atom carrying the radicals R¹ and R², can contain a further hetero ring member from the group consisting of O, NR⁷ and S(O)_m and which can be substituted by one or more identical or different substituents from the group consisting of (C₁-C₄)-alkyl, hydroxyl, (C₁-C₄)-alkoxy, R⁸R⁹N, hydroxycarbonyl, (C₁-C₄)-alkoxycarbonyl and R⁸R⁹N-CO-;

R³ is phenyl which can be substituted by one or more identical or different substituents from the group consisting of halogen, (C₁-C₄)-alkyl, phenyl, CF₃, NO₂, OH, -O-(C₁-C₄)-alkyl, -O-(C₂-C₄)-alkyl-O-(C₁-C₄)-alkyl, (C₁-C₂)-alkylenedioxy, NH₂, -NH-(C₁-C₄)-alkyl, N((C₁-C₄)-alkyl)₂, -NH-CHO, -NH-CO-(C₁-C₄)-alkyl, -CN, -CO-NH₂, -CO-NH-(C₁-C₄)-alkyl, -CO-N((C₁-C₄)-alkyl)₂, -CO-OH, -CO-O-(C₁-C₄)-alkyl, -CHO and -CO-(C₁-C₄)-alkyl;

R⁴ is (C₂-C₅)-alkyl, trifluoromethyl or phenyl which can be substituted by one or more identical or different substituents from the group consisting of halogen, (C₁-C₄)-alkyl, phenyl, CF₃, NO₂, OH, -O-(C₁-C₄)-alkyl, -O-(C₂-C₄)-alkyl-O-(C₁-C₄)-alkyl, (C₁-C₂)-alkylenedioxy, NH₂, -NH-(C₁-C₄)-alkyl, N((C₁-C₄)-alkyl)₂, -NH-CHO, -NH-CO-(C₁-C₄)-alkyl, -CN, -CO-NH₂, -CO-NH-(C₁-C₄)-alkyl, -CO-N((C₁-C₄)-alkyl)₂, -CO-OH, -CO-O-(C₁-C₄)-alkyl, -CHO and -CO-(C₁-C₄)-alkyl;

R⁵ and R⁶ are identical or different radicals from the group consisting of hydrogen and (C₁-C₄)-alkyl or the group R⁵R⁶N is a radical, bonded via a ring nitrogen atom, of a 5-membered to 7-membered saturated or unsaturated heterocyclic ring which, in addition to the nitrogen atom carrying the radicals R⁵ and R⁶, can additionally contain as a further hetero ring member an oxygen atom, a group S(O)_m or a nitrogen atom and which can carry on ring carbon atoms one or more identical or different substituents from the group consisting of (C₁-C₄)-alkyl, hydroxyl and amino and can carry on a ring nitrogen atom a radical R⁷;

R⁷ is hydrogen, (C₁-C₄)-alkyl, aryl-(C₁-C₄)-alkyl-, hydroxy-(C₁-C₄)-alkyl-, hydroxycarbonyl-(C₁-C₄)-alkyl-, ((C₁-C₄)-alkoxycarbonyl)-(C₁-C₄)-alkyl-, R⁸R⁹N-CO-(C₁-C₄)-alkyl-, R¹⁰-SO₂- or aryl, where R⁷, if this group is present on a piperazino radical representing R¹R²N, cannot be carbocyclic aryl or carbocyclic aryl-(C₁-C₄)-alkyl;

~~R⁸ and R⁹ are identical or different radicals from the group consisting of hydrogen and (C₁-C₄)-alkyl;~~

*B 1
cont*

5 R¹⁰ is (C₁-C₄)-alkyl, aryl or R⁸R⁹N;

aryl is phenyl, naphthyl or heteroaryl, which can all be substituted by one or more identical or different substituents from the group consisting of halogen, (C₁-C₄)-alkyl, phenyl, CF₃, NO₂, OH, -O-(C₁-C₄)-alkyl,

10 -O-(C₂-C₄)-alkyl-O-(C₁-C₄)-alkyl, (C₁-C₂)-alkylenedioxy, NH₂, -NH-(C₁-C₄)-alkyl, -N((C₁-C₄)-alkyl)₂, -NH-CHO, -NH-CO-(C₁-C₄)-alkyl, -CN, -CO-NH₂, -CO-NH-(C₁-C₄)-alkyl, -CO-N((C₁-C₄)-alkyl)₂, -CO-OH, -CO-O-(C₁-C₄)-alkyl, -CHO and -CO-(C₁-C₄)-alkyl;

15 15 heteroaryl is the radical of a monocyclic 5-membered or 6-membered aromatic heterocycle or of a bicyclic 8-membered to 10-membered aromatic heterocycle, each of which contain one or more identical or different ring heteroatoms from the group consisting of N, O and S;

20 20 m is 0, 1 or 2;

in all their stereoisomeric forms and mixtures thereof in all ratios, and their physiologically tolerable salts,

25 25 compounds of the formula I being excluded in which, simultaneously, R⁴ is tert-butyl or trifluoromethyl, R³ is phenyl which can be substituted by one or two identical or different substituents from the group consisting of halogen, OH, -O-R¹¹ and CF₃, R¹R²N is R¹¹-NH-, (R¹¹)₂N- or R¹²R¹³N-(CH₂)_p-NH-, p is 2 or 3, R¹¹ is saturated unsubstituted (C₁-C₄)-alkyl and R¹² and R¹³ are identical or different radicals from the group consisting of hydrogen and R¹¹ or the group R¹²R¹³N is a radical, bonded via a ring nitrogen atom, of a 5-membered or 6-membered saturated heterocyclic ring which, in addition to the nitrogen atom carrying the radicals R¹² and R¹³, can additionally contain as a further hetero ring member an oxygen atom, a sulfur atom or a nitrogen atom and which can be substituted by an aryl radical or by an aryl-(C₁-C₄)-alkyl radical, where the aryl group can be

~~substituted by one or two identical or different substituents from the group consisting of halogen, OH, -O-R¹¹ and CF₃.~~

B 1
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cont

~~2. A compound of the formula I as claimed in claim 1, in which R¹ is (C₁-C₈)-alkyl which can be substituted by one or more identical or different substituents from the group consisting of hydroxyl, (C₁-C₄)-alkoxy, (C₁-C₄)-alkyl-S(O)_m-, R⁵R⁶N and aryl, or is (C₃-C₉)-cycloalkyl which can be substituted by one or more identical or different substituents from the group consisting of (C₁-C₄)-alkyl, hydroxyl and amino; and~~

10 ~~R² is hydrogen, (C₁-C₈)-alkyl which can be substituted by one or more identical or different substituents from the group consisting of hydroxyl, (C₁-C₄)-alkoxy, (C₁-C₄)-alkyl-S(O)_m-, R⁵R⁶N and aryl, or is (C₃-C₉)-cycloalkyl which can be substituted by one or more identical or different substituents from the group consisting of (C₁-C₄)-alkyl, hydroxyl and amino; or~~

15 ~~R¹R²N is a radical, bonded via a ring nitrogen atom, of a 5-membered, 6-membered or 7-membered saturated heterocyclic ring which, in addition to the nitrogen atom carrying the radicals R¹ and R², can additionally contain as a further hetero ring member an oxygen atom, a group S(O)_m or a nitrogen atom carrying a radical R⁷ and which can be substituted by one or more identical or different substituents from the group consisting of (C₁-C₄)-alkyl, hydroxyl, (C₁-C₄)-alkoxy, R⁸R⁹N, hydroxycarbonyl, (C₁-C₄)-alkoxycarbonyl and R⁸R⁹N-CO-; in all its stereoisomeric forms and mixtures thereof in all ratios, or its physiologically tolerable salts.~~

25 *A 1*
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cont

~~3. A compound of the formula 1 as claimed in claim 1 and/or 2, in which R¹ is (C₁-C₄)-alkyl which can be substituted by one or more identical or different substituents from the group consisting of hydroxyl, (C₁-C₄)-alkoxy, (C₁-C₄)-alkyl-S(O)_m-, R⁵R⁶N and aryl, or (C₃-C₉)-cycloalkyl which can be substituted by one or more identical or different substituents from the group consisting of (C₁-C₄)-alkyl, hydroxyl and amino, and R² is hydrogen, or R¹ and R² are identical or different (C₁-C₄)-alkyl which can be substituted by one or more identical or different substituents from the group consisting of hydroxyl, (C₁-C₄)-alkoxy, (C₁-C₄)-alkyl-S(O)_m-, R⁵R⁶N and aryl; in all its stereoisomeric forms and mixtures thereof in all ratios, or its physiologically tolerable salts.~~

*A¹
Count*

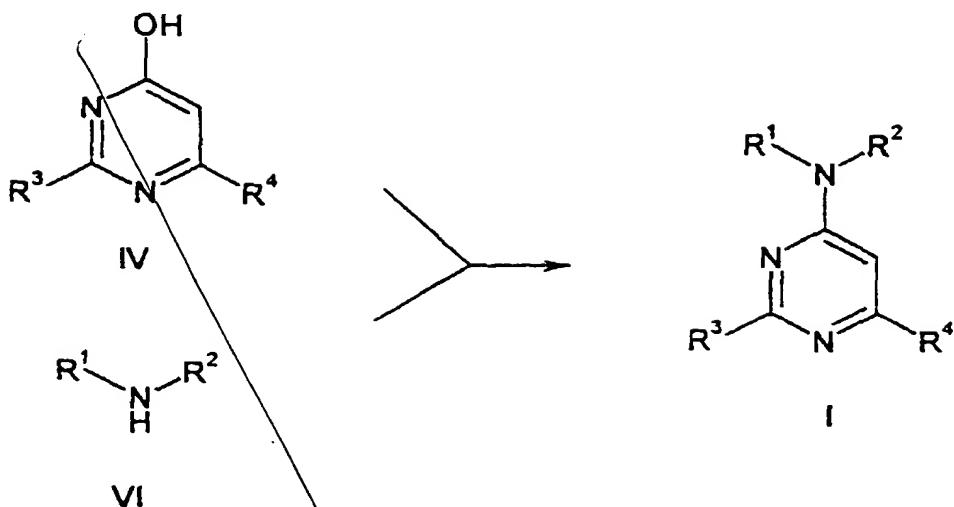
4. A compound of the formula I as claimed in one or more of claims 1 to 3, in which R¹ is (C₃-C₉)-cycloalkyl which can be substituted by one or more identical or different substituents from the group consisting of (C₁-C₄)-alkyl, hydroxyl and amino, and R² is hydrogen; in all its stereoisomeric forms and mixtures thereof in all ratios, or its physiologically tolerable salts.

5. A compound of the formula I as claimed in claim 1 and/or 2, in which R¹R²N- is an unsubstituted or substituted radical from the group consisting of piperidino, morpholino and thiomorpholino (and its S-oxide and S,S-dioxide) and piperazino; in all its stereoisomeric forms and mixtures thereof in all ratios, or its physiologically tolerable salts.

10. A compound of the formula I as claimed in one or more of claims 1 to 5, in which R³ is substituted phenyl; in all its stereoisomeric forms and mixtures thereof in all ratios, or its physiologically tolerable salts.

15. A compound of the formula I as claimed in one or more of claims 1 to 6, in which R⁴ is (C₃-C₄)-alkyl; in all its stereoisomeric forms and mixtures thereof in all ratios, or its physiologically tolerable salts.

20. A process for the preparation of compounds of the formula I as claimed in one or more of claims 1 to 7, which comprises activating a 4-hydroxypyrimidine of the formula IV and then reacting it with an amine of the formula VI,



where R^1 , R^2 , R^3 and R^4 have the meanings indicated in claims 1 to 7.

5 9. A compound of the formula I as claimed in one or more of claims 1 to 7 and/or its physiologically tolerable salts for use as a pharmaceutical.

10 10. A pharmaceutical preparation, which contains one or more compounds of the formula I as claimed in one or more of claims 1 to 7 and/or its/their physiologically tolerable salts and a pharmaceutically tolerable carrier.

15 11. A compound of the formula I as claimed in one or more of claims 1 to 7 and/or its physiologically tolerable salts for use as activators of soluble guanylate cyclase.

20 12. A compound of the formula I as claimed in one or more of claims 1 to 7 and/or its physiologically tolerable salts for use in the therapy or prophylaxis of cardiovascular disorders, endothelial dysfunction, diastolic dysfunction, atherosclerosis, high blood pressure, angina pectoris, thromboses, restenoses, myocardial infarct, strokes, cardiac insufficiency, pulmonary hypertension, erectile dysfunction, bronchial asthma, chronic renal insufficiency, diabetes or liver cirrhosis or for improving restricted learning capacity or memory power.

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